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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,208	ZAMORA, PAUL O.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-11,13-17,19-23 and 25-41* is/are pending in the application.

4a) Of the above claim(s) *29-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8-11, 13-17, 19-22, 25-28 and 40-41* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's filing of amendment/remarks on 01/18/08. By the amendment, claims 1, 8, 10-11, 13-16, 19 and 27-28 have been amended, claims 4-7, 12, 18, 24 have been cancelled, and claims 40-41 have been added. Claims 1-3, 8-11, 13-17, 19-23 and 25-41 are currently pending in the application. However, claims 29-39 are withdrawn from consideration as being drawn to non-elected invention.

2. Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3, 8-11, 13-17, 19-22, 25-28 and 40-41 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for benzyl-bis(dimethylsilylmethyl)x-oxycarbamoyl-heparin, does not reasonably provide enablement for "a cross-linkable biomolecule rendered surface adsorbable by conjugation with 1-30 hydrophobic benzylated silyl groups", "a cross-linkable biomolecule", "prosthetic hydrophobic unit and a heparin activity biomolecule" and/or "a heparin activity biomolecule". The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This rejection is maintained because the applicant's amendment has not fully overcome the rejection of the record.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The specification defines "cross-linkable biomolecule" as "cross-linkable biologically active molecule"; "heparin activity biomolecule" as "a biomolecule which includes heparin or derivative and related molecules" (page 15, lines 13-14; page 16, lines 16-17; page 17, line 5-6).

The interpretation of the instant claims allows for the inclusion of plethora agents having the desired characteristics that are known today, for example cross-linkable biomolecule such as collagen, gelatin, elastin, fibronectin, glycosaminoglycans, antibacterial, enzyme, dyes, nucleic acids, antibodies, antigens, drugs, vitamins, anticoagulant and etc…, and those that may be discovered in the future.

The specification discloses a medical device, particularly vascular graft, composed of expanded polytetrafluoroethylene where polyethylene glycol, such as bis-benzotriazole

carbonate polyethylene glycol, dissolved in organic solvent is coated on the said medical device, followed by coating of "silyl-heparin" such as benzyl-bis(dimethylsilylmethyl)x-oxycarbamoyl-heparin dissolved in second solvent and a method of making said medical device, as the specific embodiment of the invention (Examples).

It is generally recognized in the art that biological compounds often react unpredictably under different circumstances (Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)). For instance, the activity of multifunctional crosslinking agents are generally known to behave differently under different circumstances, depending upon their different binding affinity to different active molecule and different chain length of atoms between two reactive groups (see USP 6596293; USP 4665164; USP 6294697). Thus, the skilled artisan would undergo undue amounts of "trials and errors" to find out which "cross-linkable biomolecule" or "a heparin activity biomolecule" would be enabled in this specification

The relative skill of the artisan and the unpredictability of the pharmaceutical art are very high. To practice the instant invention to the claimed scope, as discussed above, applicant would have to (i) screen potentially suitable agents and (iii) assay to find out which agents are able to behave similar to the exemplified BTC-PEG and cross-linked with "`1-30 hydrophobic benzylated silyl groups" and then (iv) extrapolate the test and result to the claimed utility. In other words, the instant invention necessitates for the skilled artisan to undergo an exhaustive search for the embodiments suitable to practice the claimed invention.

Where the physiological activity of a chemical or biological compound is considered to be an unpredictable art (Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)), the skilled artisan would have not known how to extrapolate the result provided in the instant specification to the larger and highly varied genera of agents that are characterized by "a cross-linkable adsorbable biomolecule…", "prosthetic hydrophobic unit and a heparin activity biomolecule" and/or "a heparin activity biomolecule", without undue amount of experimentation.

As discussed above, given the breadth, the disparate nature of compounds that is presently claimed, the highly unpredictable state of the art where many specific differences or different physicochemical properties are existed among unrelated structural compounds or even structurally related compounds, the limited number of working examples and the insufficient amount of guidance present in the specification, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to make/use the claimed "a cross-linkable biomolecule…", "prosthetic hydrophobic unit and a heparin activity biomolecule", and/or "a heparin activity biomolecule" that would be enabled in this specification (The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether is required to make and use the instant invention. "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands, 858 F.2d

737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976))).

The examiner acknowledges that the Office does not require the present of (all) working examples to be present in the disclosure of the invention (see MPEP 2164.02). However, given the highly unpredictable state of the art and furthermore, given that the applicant does not provide sufficient guidance or direction as to how to make and use the full scope of the presently claimed invention without undue amount of experimentation, the Office would require appropriate disclosure, in the way of scientifically sound reasoning or the way of concrete examples, as to why the data shown is a reasonably representative and objective showing such that it was commensurate in scope with and, thus, adequately enables, the use of the elected species for the full scope of the presently claimed subject matter. Absent such evidence or reasoning, applicant has failed to obviate the rejection of the instant claims under 35 USC 112, first paragraph (for the lack of scope of enablement).

4. Claims 1-3, 8-11, 13-17, 19-22, 25-28 and 40-41 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new ground of rejection necessitated by the amendment filed 01/18/08.

The claims in this application introduce new limitation into the claimed invention, namely "1-30 hydrophobic benzylated silyl group". The examiner determines that when all

evidences in the original disclosure are considered and carefully reviewed, the newly amended claims fail to find support in the original specification.

Although the specification discloses benzyl-bis(dimethylsilylmethyl)x-oxycarbamoyl-heparin as the specific embodiment which has been prepared according to the procedure described in US 5955588, there is no express statement about the genus group of "1-30 hydrophobic benzylated silyl group" that can be found in the specification. Thus, the new limitation recited in the present claims, which did not appear in the specification filed, introduces new concepts and violate the description requirement of the first paragraph of 35 USC 112.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is maintained because the applicant's amendment has not overcome the rejection of the record.

Claims 19-22 recite "a conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule" and "a conjugate of from 1 to 30 hydrophobic silyl moieties and the heparin activity biomoecule", respectively. The specification does not define the term(s) and leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear. In this regard, although "benzyl-bis(dimethylsilylmethyl)x-oxycarbamoyl-heparin" (or broadly "silyl-heparin") is

disclosed as the specific embodiment(s), it is considered that the meaning of the claims should be clear from the wording of the claim alone.

Allowable Subject Matter

6. Claim 23 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614